



Regular Article

Compliance with guidelines for the perioperative management of vitamin K antagonists☆☆☆

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ABSTRACT

Introduction: Perioperative vitamin K antagonist management is an issue of concern in many countries. The availability of best practice guidelines meets health professionals' needs, but compliance is uncertain and should be assessed.

Materials and methods: Our aim was to assess practitioner compliance with the guidelines on perioperative VKA management issued by the French National Authority for Health through a national register set up in partnership with the French College of Anaesthetists and Intensivists. Seven sections of data entry were focused on perioperative management of VKAs for elective or emergency procedures. High-risk patients were identified. Compliance with guidelines was calculated per item

Results: 932 charts were completed between October 2009 and December 2010. VKA therapy was interrupted in 74% (622/837) of elective procedures and bridged in 69% cases (428/622) mainly with LMWH. According to guidelines, bridging was strongly recommended in 39% high-risk patients (175/394) but 13% of these (23/175) received no bridging. Bridging was overused in 60% of low risk patients (242/406). Other compliance rates were as follows: (i) administration of therapeutic enoxaparin doses (= 200 IU/kg/day): only 18% of high-risk patients (18/98), (ii) INR measurement on evening prior to the procedure 65% (525/803), (iii) concomitant prothrombin complex concentrate and vitamin K administration in emergency surgery 24% (21/87), (iv) postoperative therapeutic enoxaparin doses: only 20% despite widespread prescription. The incidence rate of bleeding and thrombotic events was 7.1% and 0.96% respectively.

Conclusions: These poor compliance rates with guidelines suggest that the knowledge-to-action transfer plan was inadequate and that further interventions are required.

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Introduction

Vitamin K antagonist (VKA) management is an issue of concern. The risks of poor VKA management are well known. Perioperatively, it is necessary to achieve a balance between thromboembolic risk, which on VKA interruption is greatest in high-risk patients, and bleeding risk on VKA maintenance or overdosage.

Abbreviations: HAS, French National Authority for Health; VKA, vitamin K antagonist; LMWH, low molecular weight heparin; INR, international normalised ratio.

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☆☆ This register was declared to the national commission CNIL (Nb 1397646).

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In 2008, the French Authority for Health published national guidelines aiming to reduce serious adverse events (thromboembolism or bleeding) when patients on VKAs underwent elective or emergency interventions [1]. Key recommendations were defined as follows. Patients were stratified into two risk categories for thromboembolism. The high-risk category comprised patients with (i) a MHV, (ii) atrial fibrillation with a history of transient ischemic attacks, stroke, systemic embolic event, (iii) recent (<3 months) or recurrent VTE (deep vein thrombosis or pulmonary embolism). All other patients were stratified as low risk. In an elective setting, bridging anticoagulation is recommended during interruption of VKA therapy (low molecular weight LMWH or unfractionated heparin UFH) in high risk patients whereas low risk patients do not require preoperative bridging. In an emergency setting, prothrombin complex concentrates (PCCs) and vitamin K should be administered simultaneously to correct the international normalised ratio (INR) before the procedure. Postoperatively, VKA treatment should

be resumed as soon as possible according to the thrombotic and bleeding risks. Therapeutic doses of heparin should be introduced at least 48 h following the procedure in high thrombotic risk patients until obtaining the target INR [1].

The effectiveness and implementation of guidelines needs to be evaluated. Methods including continuing medical education meetings, workshops, audit and feedback, printed educational materials have shown objective limitations on their effects on professional practice and patient outcome [2–4]. A fairly recent method of assessing compliance with good practice guidelines is the setting up of a register based on criteria drawn from standardised protocols allowing therefore the analysis of the degree of compliance with recommendations.

The aim of the present study was to assess practitioner compliance with the published guidelines through a national register set up by The French College of Anaesthetists and Intensivists, in partnership with the French National Authority for Health (HAS).

Materials and Methods

The French College of Anaesthetists and Intensivists has the agreement to validate continuing professional development (CPD) by different quality tools previously certified by the French National Authority for Health (HAS). By completing a minimum of 10 charts of the register during one year of practice, and comparing their own results with guidelines, voluntary members of the College could therefore validate their own professional practice evaluation.

The items of the register were set up by members of the working group who were involved in the guidelines development [1]. The register was available on line (Clin-Info SA Lyon France) on the website of the French College (www.cfar.org). It was declared to the national commission CNIL (Nb 1397646) which is responsible for ensuring that information technology remains at the service of citizens, and does not jeopardize human identity or breach human rights, privacy or individual or public liberties.

Practitioners had to complete 7 sections on data entry giving the following informations: demographic data, type of procedure (surgery or invasive procedure, scheduled or emergency (<12 h) procedure), indications for VKAs therapy [mechanical heart valve (MHV), chronic atrial fibrillation (AF), venous thromboembolism (VTE) or other], type of anticoagulant (fluidione, acenocoumarol, coumadin) and duration of VKA therapy, patient history, preoperative management for an elective procedure (last known INR, preoperative VKA interruption and bridging, INR measurement on the eve prior to the procedure and management if INR >1.5), preoperative management in an emergency setting (INR measurement, administration of prothrombin complex concentrates (PCCs), vitamin K, fresh frozen plasma or other antidotes), postoperative management (postoperative bridging, VKA therapy resumption), and in-hospital complications (bleeding, thromboembolism, or other).

Compliance with guidelines was assessed on the following criteria: (i) preoperatively in an elective setting: justification for VKA interruption, justification for a bridging approach, administration of therapeutic twice doses per day in patients with MHVs or atrial fibrillation when heparin bridging was required, INR measurement on the evening prior to the procedure, administration of 5 mg vitamin K if INR >1.5, and procedure scheduled in the morning; (ii) preoperatively in an emergency setting: INR measurement, concomitant injection of PCCs and 10 mg vitamin K; (iii) postoperatively: date of VKA resumption, postoperative administration of therapeutic heparin doses within 48 h, and two INR measurements separated by 24 h within the therapeutic range before stopping heparin. All these criteria fulfilled the published recommendations [1].

R language was used for descriptive statistical analysis. Results were expressed as means [95% CI] or median [range]. Percentage compliance with guidelines was calculated for the key recommendations as defined above. The expected target was 85% +/− 5%.

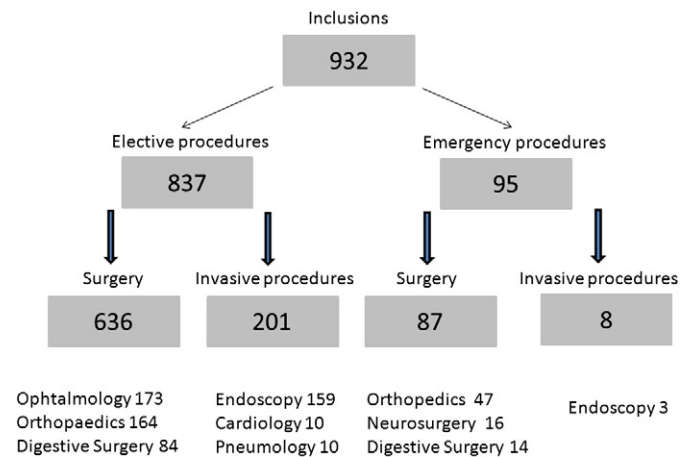


Fig. 1. Types of procedures.

Results

Demographics

A total of 79 centres entered patients into the register between October 2009 and December 2010. Overall, 976 entries were recorded (Fig. 1) and 932 were suitable for analysis. Forty four charts comprised no preoperative informations. The indications for VKA therapy and demographic data are reported on Table 1.

Preoperative Management in the Elective Setting

VKA therapy was *not interrupted preoperatively* in 26% (215/837) elective procedures. The most common elective surgical and elective invasive procedures without VKA interruption were, respectively, eye surgery (157/184, 85%) and digestive endoscopy (18/31, 58%).

VKA therapy was *interrupted preoperatively* in 74% (622/837) patients. The interval between VKA interruption and the procedure was 6 days (21%), 5 days (59%), 4 days (12%) or 3 days (6%).

One third of them (194/622) received no heparin bridging whereas 69% (428/622) received bridging mainly with low molecular weight heparin (enoxaparin). 394 patients treated for mechanical heart valve failure (58), chronic atrial fibrillation (243) or venous thromboembolism (93) were concerned. According to guideline recommendations, bridging was initiated in 152/175 patients who were classified at high-risk. However, 23 high risk patient (13%) did not receive heparin bridging (2/60 MHVs, 8/50 AF and 13/65 VTE) after VKA interruption.

Table 1
Demographic data of the 932 entries.

Age (years)	74 [95% CI: 73.6 – 75]
Sex ratio M/F	553/379
ASA Status (%)	
I	2 (1%)
II	214 (23%)
III	684 (73%)
IV	32 (3%)
VKA treatment n (%)	
Acenocoumarol	86 (9%)
Coumadine	61 (7%)
Fluidione	785 (84%)
Indications n (%)	
MHV	87 (9%)
AF	591 (64%)
VTE	191 (20%)
Others	63 (7%)

M male, F female, ASA: American Society of Anesthesiologists, MHV: mechanical heart valve, AF: chronic atrial fibrillation, VTE: venous thromboembolism.

Table 2
Bridging strategy in an elective setting according to the thromboembolic risk [1].

	High risk patient N (%)	Low risk patient N (%)
Mechanical heart valve	60	
Bridging	58 (97%)	/
No bridging	2	
Atrial fibrillation	50	345
Bridging	42 (84%)	201 (58%)
No bridging	8	144
Venous thromboembolism	65	61
Bridging	52 (80%)	41 (67%)
No bridging	13	20

Bridging in high risk patients: 152/175 (87%).

Bridging in low risk patients: 242/406 (60%).

One the other hand, bridging was overused in 60% of low risk patients (242/406) with AF and VTE [Table 2].

Low molecular weight heparin (LMWH), subcutaneous (SC) unfractionated heparin (UFH) and intravenous (IV) UFH were used for bridging in 83%, 11% and 1% respectively. Fondaparinux (not recommended) was prescribed to 23 patients (5%). Non-therapeutic doses of enoxaparin (<200 IU/kg/day) were used in 87% of all patients and in 82% of high-risk patients (80/98) receiving bridging. Enoxaparin was injected twice daily in 74% of patients.

INR was measured on the evening prior to the procedure in 65% of patients. Mean INR was 1.35 [95% CI: 1.32–1.38] in patients with preoperative VKA interruption and 2.59 [95%CI: 2.35–2.82] in patients without interruption.

The procedure was scheduled between 7 a.m. and 1 p.m. in 72% of documented cases.

Compliance with key recommendations for preoperative VKA management is summarised in Table 3.

Preoperative Management in the Emergency Setting

Among the 95 emergency procedures, 87 were surgical procedures (47 orthopaedics, 16 neurosurgery including 14 subdural or intracranial haematomas, 14 gastrointestinal, and 10 other).

The INR was known at the time of surgery in 92% of patients (80/87). Mean INR values are given in Table 4. Only 21/87 patients (24%) received PCCs concomitantly with vitamin K as recommended. All 16 neurosurgical cases received PCCs but 4/16 did not receive concomitant vitamin K. Only 4 of the 47 orthopaedics cases received PCCs but 33/47 received vitamin K alone. Practice varied even more widely for digestive surgery cases.

Only 6 of the 29 patients administered PCCs received a dose adjusted to body weight (1 ml/kg) as recommended. Median vitamin K dose was 10 mg (range 2–20). Vitamin K was administered IV in 34/59 patients (57%).

Postoperative Management

A total of 582 entries documented postoperative management after VKA interruption. They related to 28% at high risk of thromboembolism

and 72% at low risk. Postoperative heparin was administered to 447 patients (77%). Among the 135 patients receiving no postoperative heparin, 104 (77%) had received no preoperative bridging even though 17 were in the high-risk category. VKA was resumed in 70% during the postoperative observation period, in most cases within 0 to 4 days. Postoperative heparin was administered as from Day 0 in 96% high risk patients and 64% low risk patients. Enoxaparin was widely prescribed but the doses were therapeutic in 20% of cases only (Fig. 2). Half the patients given SC UFH did not receive therapeutic doses.

Postoperative heparin was not administered to 27% emergency cases. A therapeutic dose of LMWH was given to 7/67 emergency cases only.

Postoperative Complications

Among the 636 elective surgical procedures, 193 (30%) were considered at high risk for bleeding [5].

In-hospital complications were 9/932 thromboembolic events (0.96%), 67/932 bleeding events (7.1%), and 44/932 cardiovascular, pulmonary and/or septic complications (5%).

Bleeding complications occurred in 10 emergency situations and 57 elective settings. Eighteen patients required reoperation and 31 decrease in haemoglobin level > 2 g/dl were observed. VKAs were stopped in 25 patients and heparin was stopped in 24 patients. A total of 28 red blood cell packs were transfused to 36 patients. Most bleeding events were observed on the two first postoperative days.

Thrombotic and bleeding events were mainly reported in respectively 7 and 43 patients with AF. Among these, 33/43 bleeding events occurred in low thrombotic risk patients; 70% of them (23/33) received preoperative bridging whereas more than 50% of them had a high bleeding risk procedure.

Discussion

VKA management is an issue of concern. Standardized protocols for VKA management have been developed in other countries with similar recommendation of management relied to the risk category of the patients [5].

According to the above results, at least 30% of patients treated with VKAs were not receiving the care recommended by the French Authority for Health during the perioperative period. This was despite widespread promotion of the guidelines after their publication (presentations at national and regional meetings, articles in scientific journals, posting on the HAS website). Our result is in line with reports on other guidelines evaluation indicating that 20 to 40% of patients do not receive recommended care [6,7].

The most blatant deviations related to preoperative bridging. Surprisingly, 56% of low-risk patients received heparin bridging. Perrin et al. [8] found also an overuse of bridging anticoagulation in a 62 patients at low risk for thromboembolism scheduled for rhythm device surgery. They observed 3 pocket hematomas and one episode of significant bleeding reporting therefore an incidence rate of 8 % bleeding events contrasting with none thromboembolic complications. In our study, as many as 23 out of 33 atrial fibrillation patients with early postoperative bleeding were at low thrombotic risk and nevertheless

Table 3
Identification of malpractice and compliance rate with guidelines in the preoperative setting for elective procedures.

Malpractice according to guidelines	N (%)	Compliance rate with guidelines (%)
No bridging despite risk factors	23/175 (13%)	87
Bridging in low-risk patients	242/406 (60%)	40
Administration of non-therapeutic enoxaparin doses *	232/265 (87%)	23
Not twice daily injections in MHV and AF patients	49/187 (26%)	74
INR not measured on evening before procedure	278/803 (35%)	65
Surgery not scheduled in the morning	221/789 (28%)	72

VKA vitamin K antagonist; MHV, mechanical heart valve; AF, atrial fibrillation; INR, International Normalised Ratio. * < 200 UI/kg/day.

Table 4
VKA management in emergency surgery setting.

	Orthopaedics n = 47	Neurosurgery n = 16	Gastrointestinal n = 14
Mean INR [95% CI]	1.78 [1.57–1.98]	2.97 [2.35–3.60]	2.08 [1.65–2.46]
PCCs + Vit K (n)	3	12	4
Vit K alone (n)	33	0	3
PCCs alone (n)	1	4	3
Nothing (n)	8	0	3
Delay INR-Surgery (h)	13	3.6	6.5

INR, International Normalised Ratio; PCCs, prothrombin complex concentrates; Vit K, vitamin K;

received preoperative bridging whereas surgery was at high bleeding risk for most of them. Whether no-bridging would have spared these patients is impossible to assess but is a question worth asking. Widespread preoperative bridging in low-risk patients may be due to misunderstanding of the guidelines on the part of the practitioners or unjustified overcautiousness. The rationale for bridging was not explored as the primary objective of the register was to assess compliance to guidelines without influencing spontaneous practice.

Another issue of concern is that the perioperative heparin doses used in our study were not therapeutic in around 80% of the patients. This was also described in a prospective observational study including 492 patients receiving periprocedural bridging anticoagulation in 9 US hospitals. Seven centers used therapeutic doses in an average of 22% of cases as observed in our register whereas only two centers treated more than 80% of their patients with full dose heparin started a median of 1 day postoperatively [9]. Aggressive anticoagulation was significantly associated with bleeding complications. The authors reported a bleeding rate of 6.2% and thromboembolic events in 0.8% of cases. Although reduced initial doses might have been related to some considerations regarding a possible immediate postoperative increased risk of bleeding according to the attending team, this is not likely to be the case since the doses were stable over time and were not increased 48 hours postoperatively as recommended for resuming therapeutic doses according to the HAS guidelines. In our study, the overuse of bridging (even with non-therapeutic doses) associated with a high bleeding risk procedure might have contributed to early postoperative bleeding complications as observed above [8,9].

As the risks of poor VKA management are well known, we thus expected better compliance with our guidelines. Reasons that have been put forward for non-compliance are lack of practitioner awareness owing to information overload, guidelines considered inapplicable in clinical practice, lack of visibility on expected outcomes, lack of appropriation or motivation, and resistance of patients, their family or environment [10–13]. In addition, the supporting evidence is often subject to considerable bias and consequently suspicion, and guideline implementation is seldom assessed [14,15]. Awareness that research

findings are not making their way into practice in a timely fashion is growing, and ways to minimize the so-called knowledge-to-action gap are needed although little is yet known on how to improve care in many settings [16]. In the Deming cycle, monitoring knowledge use – in our case instrumental use – is a key step in improving quality of care. Good compliance would depend on sustained monitoring after identification of a precise target, and it may thus be wishful thinking to expect an 85% compliance rate with our multiple targets. However, in a three-hospital healthcare system in the US, a strategy focused on improving anticoagulant safety across the continuum of care resulted in a significant reduction in adverse events [17]. Boosting implementation by passive information dissemination is generally thought to be ineffective in changing practices, whereas combining several types of intervention, as we did, is better [18]. However, promotion of our guidelines by HAS and the French College of Anaesthetists and Intensivists among potential users seems to have been inadequate. Further interventions are doubtless needed. For instance, computerized reminders may prove useful in a setting as complex as perioperative VKA management [15]. Other means have been recently proposed by the French College of Anaesthetists and Intensivists to improve compliance including on line prescription tools and clinical cases with MCQs referring to guidelines, organization of interactive topics during national meetings.

Some limitations might be highlighted. Guidelines related to perioperative VKA management are based in large part on “expert” opinion because the lack of high level evidence in both French and US recommendations especially for bridging anticoagulation (grade 2C in [5]). One can therefore query their relevance to the practitioner. This limitation was discussed in a recent editorial published by Hessel and Levy [19]. They pointed the need for more high level evidence studies allowing more enthusiastically endorsement by clinicians. Other limitations of our results may be related to the nature of this declarative study. The objectives were not to enroll consecutively all the patients with VKA treatment during one year period but to incite voluntary members of the French College of Anaesthetists and Intensivists to assess their own practice through a fairly recent method of evaluation which could lead them to validate a process of professional practice evaluation. The validity of the results may be questionable as consecutive patients were not included and no specific monitoring provided. However as for all surveys of spontaneous declaration, the exact incidence of any incident cannot be accurately determined but effective signals of risk, in this case, poor practice management can be efficiently identified. Moreover, our results probably overestimate the compliance with guidelines as they were provided by practitioners interested by the challenge of perioperative VKA management. Thus general malpractice in our country might be even worse than that reported by the responders to our register which highlighted specific points of putative progress.

The development of new oral anticoagulants, with an allegedly reduced incidence of adverse events in large clinical trials, may prompt new guidelines, but should not put off implementation of measures to improve compliance with the recommendations on existing VKAs which continue to be administered to large numbers of patients especially for MHV [20,21]. These new oral anticoagulants still have to undergo strict post-marketing surveillance to avoid patients being at risk of premature complications. Setting up a new register might be a fair method of evaluation of practice which could be extended to other countries.

Conflict of Interest Statement

None related to the study for all the authors.

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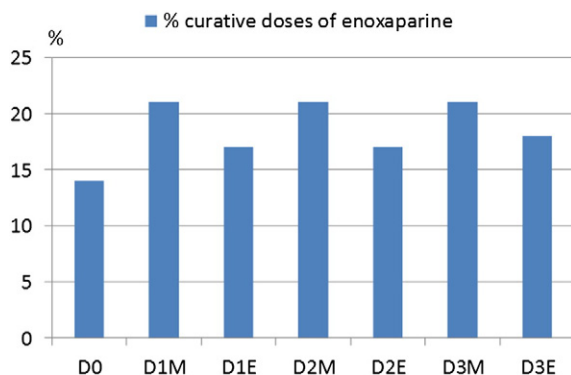


Fig. 2. Compliance (% of patients) with postoperative administration of therapeutic enoxaparin doses (D0–D3: Day 0 to Day 3; M: Morning; E: Evening).

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